Exhibit 3

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

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IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM, PRODUCTS LIABILITY LITIGATION	:MDL NO. 2327 : :VOLUME II :

THIS DOCUMENT RELATES TO ALL CASES AND
VARIOUS OTHER CROSS-NOTICED ACTIONS
CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

- - -

January 8, 2014

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Transcript of the continued deposition of THOMAS A. BARBOLT, Ph.D., called for Videotaped Examination in the above-captioned matter, said deposition taken pursuant to Superior Court Rules of Practice and Procedure by and before Michelle L. Gray, a Certified Court Reporter, Registered Professional Reporter, and Notary Public, at the offices of Riker Danzig Scherer Hyland & Perretti LLP, Headquarters Plaza, One Speedwell Avenue, Morristown, New Jersey, commencing at 9:07 a.m.

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BY MR. THORNBURGH:

Q. Did you look at any -- any of the explant reports that Ethicon received that showed that women who had mesh devices explanted, also, some of those women had ulcerations?

MR. THOMAS: Object to the form of the question.

THE WITNESS: There would be a clinical explant, and I have not reviewed any of that information.

BY MR. THORNBURGH:

Q. You have also been designated as the 30(b)(6) witness to discuss the specifics of all testing related to TVT products during the design, development stages, including but not limited to porosity testing, particle loss, degradation, and leaching. We'll shorten that up.

You have also been designated as the Ethicon person who will testify regarding all testing related to the TVT products and particle loss. Correct?

A. Yes, that's correct.

MR. THORNBURGH: Off the record.

THE VIDEOGRAPHER: Off the video record, 3:18.

(Short break.)

THE VIDEOGRAPHER: Back on the video record, 3:24.

BY MR. THORNBURGH:

Q. Doctor, I want to mark as -- give me one second.

There we go. I am going to mark as Exhibit Number 2255 an e-mail dated February 27, 2004.

(Document marked for identification as Exhibit T-2255.)

BY MR. THORNBURGH:

Q. This is an e-mail from Dan Smith to a number of -- or to Janice Burns dated February 27, 2004, discussing issues with TVT and particle loss. Right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I've not seen this memo, and I am not sure that it relates to the biocompatibility or particle loss in a preclinical arena. I have to read through here --

MR. THOMAS: I think they showed it to you at your last deposition.

MR. THORNBURGH: Yeah.

THE WITNESS: Okay.

BY MR. THORNBURGH:

Q. And it will relate preclinically.

A. Okay. Fine.

Q. We'll talk about it and refresh in the preclinical context.

A. Okay. Fine.

Q. Now, this is a document that discusses problems with particle loss that were being experienced -- were experienced by Ethicon regarding its TVT products, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I'm sorry. I was kind of reading through here, and I see that I have looked at it before.

Could you please repeat that question?

BY MR. THORNBURGH:

Q. Yeah. This is an e-mail from Dan Smith to Janice Burns which discusses problems of particle loss that were being seen by doctors in the field who were using the TVT product, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Yes. That's what it looks like.

BY MR. THORNBURGH:

Q. And in that context, Dan Smith says: This is not going away any time soon, and competition will have a field day. Major damage control offensive needs to start to educate reps and surgeons upfront they -- that they will see blue shit, and it is okay. This is why I wanted to launch TVT-O in clear.

Do you see that?

A. Yes.

Q. And when you worked for -- as Ethicon, you recognize that there is -- at least during the mechanical cut days of TVT mesh, there was a problem with particles falling away from the mesh, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Yes.

BY MR. THORNBURGH:

Q. In fact, that same month -- I've handed you what's been marked as Exhibit Number 2256.

(Document marked for identification

as Exhibit T-2256.)

MR. THOMAS: May I have one, please?

BY MR. THORNBURGH:

Q. That same year, in November of 2004, Ethicon received an e-mail concerning complaints from Dr. Eberhard.

It says: Dear all, please see attached below a letter with pictures of competitor's device and its translation from Dr. Eberhard, an important customer in Switzerland, regarding mesh fraying. Regarding the mesh frayed complaints, decision is not open corrective action -- a decision to not open corrective action is based on the following memo. Could you please give feedback?

So this is an e-mail regarding Dr. Eberhard, who had written a letter to Ethicon regarding problems with the mesh devices, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Yes. It looks that to be the case.

BY MR. THORNBURGH:

Q. And David Menneret on November 9th -- of November 12th of 2004 wrote that: We already

received similar complaints. This kind of issue is usually attributed to over-tensioning of the tape during the procedure. Fraying is inherent in the product based on the mesh construction. When any amount of tension is applied to the mesh, fraying occurs. Stretching of the mesh increases the probability of fraying.

Do you see that there?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Yes.

BY MR. THORNBURGH:

Q. I am going to put it in the scope of the deposition. So according to David Menneret, one of the problems with fraying and particle loss was from tensioning of the mesh and specifically tensioning of the TVT tape or the tape that was being used by Ethicon, correct?

MR. THOMAS: Same objection.

THE WITNESS: Yes. I think that's what they're referring to.

(Whereupon, a discussion was held off the record.)

(Document marked for identification as Exhibit T-2257.)

BY MR. THORNBURGH:

Q. What's been marked as Exhibit Number 2257 is a document or a fax that was received by Basso Sibylle to David Menneret, who said: Attached is Dr. Eberhard's letter regarding TVT blue tape.

Do you see that?

A. Yes.

(Document marked for identification as Exhibit T-2258.)

BY MR. THORNBURGH:

Q. I've marked as Exhibit Number 2258 the translated letter from Dr. Eberhard, who writes: Dear Emilie, Business Unit Manager Gynecare Switzerland. Please find attached a TVT tape which was used as a demo unit for patients before they had their operation. Already at the operation, it is embarrassing to see how the tape is crumbling. It gets worse if there is stretch on the tape.

I can't understand that no one will solve the problem for such a long time. At least as the tape has becoming blue, everyone has realized that the quality of the tape is terrible. A tape has to be weaved and should not crumble. Please try one and you will see that the tape is crumbling.

Did I read that correctly?

MR. THOMAS: Object to the form; scope.

THE WITNESS: Yes.

(Document marked for identification as Exhibit T-2259.)

BY MR. THORNBURGH:

Q. Marked as Exhibit Number 2259 a compilation of e-mails --

MR. THOMAS: May I have one, please?

MR. THORNBURGH: I'm sorry, Counsel.

BY MR. THORNBURGH:

Q. -- a string of e-mails in which Charlotte Owens was one of the recipients and authors of the e-mails.

Do you know who Charlotte Owens is?

A. I think we overlapped a little bit. Obviously, she is a medical director of Gynecare.

Q. So she was in charge, the director of the medical affairs part of Ethicon, right?

A. Yes, for Gynecare.

Q. For Gynecare.

And she received, according to this document, an e-mail from Dan Smith, who appears to have included an e-mail or an excerpt from something

authored by Steve Bell of Gynecare.

It says: Dear all, as more and more customers now move to TVT blue and TVT-O with blue mesh, you may sometimes hear, I can see small blue pieces come off the mesh. What's wrong?

The key points, it says, number two, the same -- number one, Gynecare blue TVT mesh and Gynecare clear TVT mesh are exactly the same.

Number two, the same number of particles came off the clear mesh when it was stretched.

Do you see where it says "when it was stretched"? Do you see that?

A. Yes.

Q. Okay. It's just that you see them against the tissue and skin more when they are blue. This is no different to what has happened in the past seven years with TVT.

Reassure your doctors that this is part of the success of TVT. The way we have cut the mesh makes the edges softer, and we feel that this has been a crucial success factor in TVT. Reassure that Prolene has proven to be inert.

Do you see that? "Proven to be inert." Right?

A. Yes, I see that.

Q. In summary, be proactive. The competition will try to target this, especially Bard, as they have a sealed edge tape, and remind your customers it is the same as clear. It is proven safe implant. In the blue format over 100,000 have been implanted worldwide. Remind them that the benefits -- of the benefits of blue mesh. Remind them it is inert Prolene with over 25 years of health. Remind them our wealth of clinical data with ultra low complication rates.

Do you see that?

A. Yes. I can read it.

Q. Okay. So number one is -- there's particle loss being seen when the tape is stretched. Do you see that?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Yes, I see it.

BY MR. THORNBURGH:

Q. Okay. And, number two, we know from what we've seen in the internal studies by Ethicon that the Prolene in the TVT mesh is susceptible to surface degradation, correct?

MR. THOMAS: Object to the form of

the question.
BY MR. THORNBURGH:
Q. Yes, Doctor?
A. Yes.
Q. This doesn't -- this summary doesn't say remind physicians that Prolene mesh is susceptible to surface degradation, does it?
A. I don't know that I should be even commenting on this exchange between a marketing person and the field.
Q. Well --
A. First, he's not a scientist. Second, I am not sure what it's got to do with the preclinical data that we brought here to talk about.
Q. I am going to put it all into context. I assure you.
A. Okay.
Q. But it says -- it doesn't say remind physicians who are purchasing these permanent implants which are going to be put into -- in and around the vaginal area of the woman's body, that the surface area or the surface layer of the Prolene in the TVT is susceptible to surface cracking or surface degradation, right?
MR. THOMAS: Object to the form of

the question. Scope.

THE WITNESS: I want to make a distinction between particles shed from the mesh, which I consider a macroparticle, and the kind of microparticles that you're alluding might shed from or as a result of some sort of surface cracking observed on the Prolene fiber. Two different issues.

BY MR. THORNBURGH:

Q. Both --

MR. THOMAS: Are you finished?

THE WITNESS: Yeah.

MR. THOMAS: Sorry.

BY MR. THORNBURGH:

Q. Both of which, by themselves, can elicit a -- an inflammatory response.

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. In fact, nanoparticles or microparticles will excite macrophages more than macroparticles will.

MR. THOMAS: Which question do you want him to answer?

BY MR. THORNBURGH:

Q. Correct?

MR. THOMAS: Which question do you want him to answer? You posed two of them.

MR. THORNBURGH: Both.

MR. THOMAS: One at a time.

MR. THORNBURGH: My last one first.

THE WITNESS: So the first part, the fragments that we've talked about that have been observed alongside the suture and in what I call macroparticles have a tissue reaction to them very similar to the polypropylene fiber.

And the second question in terms of these microparticles that I make reference to that you allude would come off the surface as a result of surface cracking, there's been no evidence in any of the 49 documents that I've brought today that there's an increase in tissue reaction over time. And, in fact, in many studies, there's a diminution of the tissue reaction over time. So there's no evidence to support that second piece.

BY MR. THORNBURGH:

Q. The truth is the testing that you and Ethicon were doing preclinically was really marketing studies. They were studies to -- that were being conducted because of the threat from

competitors like Bard.

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Absolutely not. The preclinical studies conducted by Ethicon were either for regulatory submission or for internal information to advance product development.

BY MR. THORNBURGH:

Q. When you did rabbit studies that looked at particle loss in rabbits, the tape that was being implanted in the rabbits was not undergoing the same type of stresses and strains that the tape undergoes in the human environment or the human condition when the device is being implanted, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: As I recall in that study -- and we could make reference to it, and I probably should go to it -- that they implanted the mesh in a manner that the mesh might be implanted in patients; that is, insertion, passage through muscle, which would offer up some tension, and then implantation.

BY MR. THORNBURGH:

Q. It's not the same implant condition that is occurring in women who are having these implants put in their bodies for the rest of their lives --

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. -- right?

MR. THOMAS: Scope.

THE WITNESS: I don't know all the parameters of that condition that you make reference to, okay, because I suspect that each patient has different issues.

And this study was an attempt to make the implantation procedure very consistent so that we could determine whether or not there is stretching of the tape or deposition of particles in the surrounding tissue.

BY MR. THORNBURGH:

Q. You didn't answer my question completely.

It's not the same implant condition that is occurring in women who are having these implants put into their bodies for the rest of their lives.

MR. THOMAS: Object to the form of the question; scope. And, also, he did answer your question.

BY MR. THORNBURGH:

Q. Well, number one, rabbits are quadrupeds, not bipedal, right?

A. Well, I thought we were talking about the conditions of implantation, and it would have nothing to do with the number of legs.

Q. Well, we're talking about -- we're talking about the condition, the real human condition, compared to the animal condition where you conducted these studies.

MR. THOMAS: He's not a clinical guy.

MR. THORNBURGH: Number one -- I think he can say pretty easily that rabbits are bipedal -- or quadrupeds, not bipeds.

BY MR. THORNBURGH:

Q. Right?

A. I said I don't know all the conditions in the clinical situation that you're alluding to and whether or not they would compare with the passage of mesh through skeletal muscle of rabbit.

Q. Your rat study, which has previously

been marked as T-2133, ETH.MESH.05316775 --

MR. THOMAS: Which one are we talking about, Dan?

MR. THORNBURGH: Sorry.

MR. THOMAS: Which study?

MR. THORNBURGH: Yeah. The histological evaluation and comparison of mechanical pullout strength of Prolene and Prolene Soft mesh in a rabbit model.

Let's go ahead and mark it as an exhibit.

It's already been marked, Exhibit Number 2133. Sorry. 2133. It was marked at a prior deposition.

MR. THOMAS: Oh, okay.

Do you have another one?

MR. THORNBURGH: Yeah, I do. Sorry. I think I left the extra copy -- oh, found it.

2133.

BY MR. THORNBURGH:

Q. Now, Ethicon was concerned about the -- what the competition would say about the TVT products as a result of the particles that were being seen with the TVT blue, correct?

MR. THOMAS: Object to the form of

the question; scope.

THE WITNESS: Yeah. And I guess I can't really address what Ethicon was thinking and why they did stuff, only to -- insofar as it reflects the documents that we brought here today to talk about biocompatibility or any preclinical studies.

BY MR. THORNBURGH:

Q. So you conducted a 14-day rabbit study, right?

A. Ethicon conducted such a study.

Q. And women who have these devices implanted in their bodies are -- the intention is that these implants will remain in their bodies for the rest of the woman's life, correct?

A. Yes.

Q. Now, how much mesh -- what was the size of the mesh implanted in the rabbits?

A. The mesh was -- the TVT tape width, about 10 millimeters. That's what was implanted. And samples of Prolene Soft mesh and ultrasonically cut mesh were done in a very similar way.

And as I look on Page ETH.MESH.05316780, the intention was to leave 3 centimeters of that mesh within the epaxial

musculature.

Q. Okay. And how much mesh is implanted in women during the implant process?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I don't know that number. That's a clinical issue, and it would depend on which TVT product you're talking about.

BY MR. THORNBURGH:

Q. Well, the more mesh, the more particles there are to flake off of the mesh device, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I don't know that for certain.

BY MR. THORNBURGH:

Q. You don't know that?

A. No.

Q. Did you look at the Pariente study before you came here today?

A. No.

Q. Do you recall discussing the Pariente study during your deposition last time?

A. The name sounds familiar.

Q. Do you recall that in the Pariente study, it was found that 8.5 percent of the particles in the TVT mesh fell away from the TVT product?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I don't recall that information.

BY MR. THORNBURGH:

Q. Did any of your studies try to mimic the stresses and strains that were used in the Pariente study during the implantation of the mesh in rabbits, and in this case, in rabbits for 14 days?

MR. THOMAS: Object to the form of the question; scope.

Do you have one to show him?

THE WITNESS: Was it a clinical study or a preclinical study?

MR. THOMAS: That's why I want you to see it.

MR. THORNBURGH: It was an ex vivo study.

THE WITNESS: It could be ex vivo from animals or humans.

BY MR. THORNBURGH:

Q. Do you know sitting here today whether the studies that you did were -- whether or not you used the Pariente study to determine particle loss in any of the studies that you did?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: It's not indicated in the study report, any reference to the Pariente study.

BY MR. THORNBURGH:

Q. What loads were used when implanting the 3-centimeter by 1-centimeter samples in these rabbits?

MR. THOMAS: Object to the form of the question.

THE WITNESS: As indicated in the study report, the mesh was drawn through the epitaxial musculature, and whatever forces that would offer the mesh, that's what happened.

BY MR. THORNBURGH:

Q. And can you hold up for the ladies and gentlemen of the jury approximately 3 centimeters?

A. Maybe an inch and-a-half.

Q. So your study in rabbits was about an inch and-a-half piece of mesh that was implanted in the muscle of the rabbit for 14 days max, right?

A. That's correct.

Q. Did you measure the force by Newtons or the load by Newtons that would be used or was used during the implantation process to determine whether or not it would mimic the implantation conditions in human women?

A. No assessments of force required to implant the mesh samples was recorded, only the explant tensions.

Q. Do you know what forces are used during the implantation process in women?

MR. THOMAS: Object to the form of the question. Scope.

THE WITNESS: It is a clinical question.

BY MR. THORNBURGH:

Q. Well, isn't that -- isn't that clinical information important when you're trying to determine particle loss in rabbits?

A. This preclinical study was an attempt to simulate implantation in patients. And it is what it is.

Q. Well, then, you didn't consider the level of force used when implanting a TVT-Retropubic in women to try to mimic the same loads being applied to the one and-a-half inch piece of mesh that you're implanting in these rabbits, did you?

A. I can't speak to anything that was done in the clinical environment.

Q. Did you ask anybody from the clinical environment: Hey, you know what? We want to try to, in the preclinical environment, to test this issue. We want to determine the amount of force or loads that are being applied during the implantation of a larger piece of mesh in women so that we can mimic that condition in the preclinical studies that we're doing with one and-a-half piece of mesh?

A. That was not done --

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. You did not. Did you have any discussions with anybody in the clinical arena to determine the implant conditions in women to try to mimic those implant conditions in the animals that you were testing this mesh in?

A. That's not indicated in this report.

Those discussions may have taken place.

Q. Did you do that? Did you try -- did you understand or try to understand the amount of force or loads in any of the studies that you did in -- that were -- that were needed for implantation in women so that you could mimic the same implant condition in your preclinical studies?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Again, you're talking about data that would be collected in a clinical environment, and I am not here to address that other than the preclinical data that we brought and anything that's relevant to it.

BY MR. THORNBURGH:

Q. Did you discuss with anybody for any of the preclinical studies or before you walked in here today what the implant conditions are like in terms of a force required to implant the stretching that's done during the implant procedure so that you could gain a better understanding of your preclinical studies?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's the kind of

information that would be in the clinical arena, and that's not part of what I am here to discuss.

BY MR. THORNBURGH:

Q. But you didn't discuss with anybody in the clinical arena whether or not the preclinical studies that you're trying to rely on now were done in a condition that would mimic the human implant condition?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I think I've answered that three times, and the same answer I'll give now, and that is this information would be collected in a clinical environment and is not part of what I am here to discuss.

BY MR. THORNBURGH:

Q. Let's go ahead and mark as Exhibit 2260 the Pariente study.

(Document marked for identification as Exhibit T-2260.)

MR. THORNBURGH: Dave, I have a copy for you, and I just don't have -- it's not stapled.

MR. THOMAS: That's fine. Thank you.

BY MR. THORNBURGH:

Q. You've seen this study before,

haven't you?

A. I think I have, but it doesn't look so familiar. The name does seem familiar, but I'd have to read through it to see what happened here.

Q. Do you want to take a moment and look at it?

A. Sure.

Okay. This looks like an in vitro study.

Q. Did you look at this study before you came in here today?

A. No.

Q. You don't recall looking at the study with me during your prior deposition?

A. Again, I think the name rings a bell, but I've looked at a lot of studies.

Q. Okay. Well, in the Pariente study, the investigators were looking at -- as their endpoint or one of their endpoints, particle loss, correct?

A. Yes.

Yes, I recall the study now. This one we discussed during the last deposition.

Q. And it says here: To evaluate the shedding of particles, each sample was weighed

before and after soft procedure, and values range from 0 to 8.5 percent of initial weight.

Did you -- in any of your studies, did you weigh the sample pre and post procedure?

A. No.

MR. THOMAS: Pre-implant?

BY MR. THORNBURGH:

Q. Pre-implant and post explant.

A. No. That would not be practical, because there would be tissue adherent to the mesh, and it would alter its weight.

Q. So you didn't look at the weight to determine particle loss, did you?

A. No. But we looked at something more important than that in the study that we discussed earlier, and that is whether or not particles were observed in the immediate vicinity of the implant.

Q. You didn't look at weight, did you?

A. No.

Q. You didn't determine the percent of particle loss in any of your studies, did you?

A. As I pointed out --

Q. It's a yes or no question.

A. As I pointed out, weighing a mesh after implantation would not be useful, because

there would be additional weight of tissue adherent to it.

Q. It could dissolve the tissue, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That would be a possibility.

BY MR. THORNBURGH:

Q. So you could have weighed it after dissolution or dissolving -- desiccation of the tissue, right?

A. That's possible. That could introduce other things that you would have to control for, but, clearly, there's no end to the number of studies that could be conducted.

Q. But you didn't do that study, did you?

A. No.

Q. And you didn't determine the percentage of particle loss, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's correct.

BY MR. THORNBURGH:

Q. The study goes on to say: During

surgical use, these articles are released in soft tissue, and it is not possible to know where they go.

MR. THOMAS: There's no question pending.

BY MR. THORNBURGH:

Q. Do you see that?

A. Yeah, I see it.

Q. And that's true? When particles are released into soft tissue, they can migrate, can't they?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's not very likely. With any particles, any macroparticles that would be adherent to the mesh or they might flake off the mesh in vivo, they would reside in the immediate vicinity of the implant, and they would be surrounded by connective tissue, just like each element of the mesh.

BY MR. THORNBURGH:

Q. When I get a splinter in my finger, no matter how deep it is, my body's -- my body's inflammatory response to that little tiny piece of splinter will push that splinter out of my body,

migrate it from where it found itself initially until it's outside of my body, won't it? That happens, doesn't it?

A. That can happen if it's close enough to the surface of your skin.

Q. So migration of particles is possible as a result of the inflammatory process that's taking place in the human body, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Highly unlikely.

BY MR. THORNBURGH:

Q. And that's based on what, sir?

A. My experience looking at implanted materials and the experience from the Prolene suture NDA, which calls out macroparticles of the suture, likely resulting from a swaging process of macroparticles that got adhered to the suture, and they got implanted inadvertently with the suture.

And what's observed is that there's a tissue reaction around the filament of the suture and then adjacent to it, the particle, or the very similar reaction around it.

There's no evidence that that particle will migrate away from the fiber from which

it might be associated with.

Q. During surgical use, these particles are released in soft tissue, and it is not possible to know where they go.

That's what these authors write, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: That is the opinion of these authors.

BY MR. THORNBURGH:

Q. When these authors tested particle loss, they found that the TVT lost the most particles of all the things that were tested, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Under the conditions of their testing, that's the case.

BY MR. THORNBURGH:

Q. And they found that TVT lost 8.5 percent of the particles, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I think -- I think they

mean 8.5 percent of the weight was lost as particulates.

BY MR. THORNBURGH:

Q. Yeah. I'm sorry. They found that 8.5 percent of the weight of the TVT sling was lost to particles, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I think that's what they're saying.

BY MR. THORNBURGH:

Q. Almost 10 percent of the TVT sling was lost in their study through particle loss, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Eight and-a-half percent.

BY MR. THORNBURGH:

Q. Now, what loads were used to test TVT particle loss?

MR. THOMAS: In what context, Dan?

MR. THORNBURGH: In this study.

MR. THOMAS: In which study?

MR. THORNBURGH: The Pariente study.

MR. THOMAS: Thank you.

BY MR. THORNBURGH:

Q. Measured in K per Newton. Do you know what that means? Peak load?

A. Well, I'm just looking at the text where they talk about a soft procedure, and I'm looking for the data that would be corresponding to it.

Q. I think if you look here, maybe this might help.

Do you see Table 1?

It shows low deformation curves?

A. No. It looks like they gave each material a different load.

Q. Starting at?

A. TVT at .041 ranging to .012 for I-Stop.

Q. Do you know how much load is used in the implantation of the TVT?

A. I do not.

Q. Do you know how much load you used when you implanted the 1.5 by -- 3-centimeter by 1-centimeter piece of mesh in the rabbits use study?

A. That was not measured.

Q. You don't know sitting here today if

the loads that you used would have mimicked the loads used during the implantation of TVT in an actual woman, right?

A. Well, as I mentioned four times previously, that would be data coming from the original -- the clinical arena, clinical environment, and it's not what I am here to address.

Q. And that information wasn't important for you when you designed the studies that looked at particle loss, was it?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Obviously, it was not considered necessary to execute this protocol.

BY MR. THORNBURGH:

Q. You would agree that if 8.5 percent of particles are being lost during the implant procedure on the TVT mesh, that that would increase the inflammatory response.

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Highly unlikely, given the mass of material implanted as part of a tape.

Think about all of the monofilaments woven into a mesh, and think about some particulates

lying adjacent to the implant. It would have the same kind of tissue reaction. It would be probably not discernable against the background of implantation of a mesh, even if it had no particles.

(Document marked for identification as Exhibit T-2261.)

BY MR. THORNBURGH:

Q. I marked as Exhibit Number 2261 a side-by-side photograph of the -- a document that includes a side-by-side photograph of mechanical cut TVT mesh and laser cut TVT mesh.

Have you seen this before?

A. I don't think so.

Q. Do you see where it says side-by-side relaxed after 50 percent elongation?

MCM would mean mechanical cut mesh, right?

A. Yes.

MR. THOMAS: Object to the form of the question; scope.

All of this is beyond -- excuse me. All of this is beyond what he's been designated for.

MR. THORNBURGH: No, it's not.

BY MR. THORNBURGH:

Q. LCM is laser cut mesh? Do you see

that?

Do you see that?

A. I understand it's outside my area.

Q. What -- what? No, it's not. I am going to put it in context.

What percentage of elongation was used in any of your studies to determine particle loss?

Did you ever measure the elongation that was being applied during the implantation of this device in any of the preclinical studies that you conducted?

A. This might be the sixth time that I've responded to that question, and it's the same.

This is data that would be acquired in the clinical environment and is not part of the preclinical database that I'm here to discuss.

Q. No. I asked you a different question. My question was: In any of the preclinical studies that you did or that Ethicon did to look at particle loss and tissue reaction, did you ever look at or record the percentage of elongation during the implantation in the animal study?

A. Not that I'm aware of.

Q. Do you see where it says degradation?

MR. THOMAS: Where? What page are you on?

MR. THORNBURGH: I'm on the side-by-side image of the MCM versus LCM.

BY MR. THORNBURGH:

Q. You were designated as somebody that would talk about evidence and studies regarding degradation, right?

MR. THOMAS: We provided the studies on which he's prepared to testify. This is not one of the documents.

MR. THORNBURGH: You only provided studies that would support your position, not studies that would show that your position was incorrect.

MR. THOMAS: Now, we invited you to ask him to review other things you wanted to be prepared on, and you didn't. So this is -- if you want him to be prepared on it, he'll study it and come back with an appropriate answer. He's not prepared on it today.

BY MR. THORNBURGH:

Q. Do you see where it says degradation, Doctor?

A. I am not prepared to respond to those questions today. It is not part of the preclinical data package that I put together to address degradation questions.

Q. You see where it shows the particles that were lost? Do you see that? Do you see all those flakes?

A. I can see particles in the photograph.

Q. You're not suggesting to the ladies and gentlemen of the jury that there won't be an individual inflammatory response to each one of those particles in tissue?

A. It would pale by comparison to the tissue reaction from the implanted tape.

Q. But there will be an increased inflammatory response or an inflammatory response to the individual particle, correct?

A. There will be an inflammatory response to that individual particle, but it will not be appreciated against the inflammatory response of the entire case.

Q. The phagocytes will try to gobble up that foreign body, won't they?

A. One will not be able to differentiate

contribution of a particle to the overall reaction to the entire tape.

Q. Inflammatory cells would be released to attack that particle, to try to rid the body or the animal of those particles, correct?

A. The tissue reaction to these particles would be no different to the tissue reaction to any filament in any part of the mesh.

Q. But there will be a tissue reaction, right?

A. Yes.

Q. And when you increase the surface area of a foreign body, that will increase the body's inflammatory response, won't it, sir?

A. Any increase in tissue reaction will not be perceptible against the background of tissue reactions of the implanted tape.

Q. When you increase the surface area, you increase the inflammatory response. Right, Doctor?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's a general -- that's a general principle.

BY MR. THORNBURGH:

Q. And the principle is true. The principle -- the answer to that principle would be yes. When you increase the surface area, you increase the inflammatory response.

A. Not in this case.

Q. In all other cases except for cases against Ethicon products?

MR. THOMAS: Object to the form of the question.

THE WITNESS: In any case where the addition of particles -- in any case where the addition of the inflammatory reaction to a particle could be perceived against a tissue reaction of the implanted tape itself would be insignificant and unappreciable.

BY MR. THORNBURGH:

Q. General scientific principle is when you increase the surface area, you increase the inflammatory response, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's a general scientific principle.

MR. THORNBURGH: Off the record for a minute.

MR. THORNBURGH: Objection.

THE WITNESS: No.

BY MR. THOMAS:

Q. The next section that I have in this disclosure, which is T-2262, is the specifics of all testing related to TVT products during the design and development stages, including particle loss.

Now, tell me the difference between the clinical and the preclinical analysis of particle loss.

MR. THORNBURGH: Objection.

THE WITNESS: The preclinical assessment of particle loss is one that can be done in any implantation study where the implant is visualized against the surrounding tissue. And if there are any particulates there, they would be observable.

I am not sure about the clinical arena. I don't know that I can speak to that.

BY MR. THOMAS:

Q. Okay. The clinical arena involves humans, and that's not work that you do?

A. That's correct.

Q. And you are aware of the particle loss issues insofar as they relate to preclinical

testing?

A. Yes.

Q. And why did you pick the documents that you have here, beginning in 1964, the 38 documents, going all the way up to 2007? Why did you include those?

A. Particles were observed in the Prolene suture NDA submission. And as I pointed out this morning, they resulted in an inflammatory reaction very similar to that reaction around the filaments of the suture.

Q. You talk about fragments and you've talked about particles. Are fragments and particles different?

A. As I mentioned this morning, I see a big difference there.

A fragment of a suture is likely to have been related to the swaging process or the cutting lengths of suture, or a fragment of suture gets attached to the suture and then gets implanted with it.

That's different than the microparticulates that we discussed earlier, looking at data from the seven-year dog study.

Q. And so the 38 studies that you've

included in your section of particle loss from the period, 1964 to 2007, you've looked for the extent to which there's been any adverse consequences noted in preclinical studies from any kind of particle loss of sutures and mesh?

A. Yes, although fragments are noted in the NDA submission and in the Postlethwait study that we discussed earlier. In the early going, in the development of Prolene suture, I've not seen personally in any of the implantation studies that I've conducted any sort of fragment of filament next to a filament in an implantation study.

Q. And you talked before about the particle in the NDA study and the kind of reaction that -- tissue reaction with respect to that particle.

With the particle in the NDA study, did you find any adverse inflammation or tissue reaction that had any consequences to you for a preclinical perspective?

A. No.

Q. Why?

A. It was the same kind of reaction around the fragment as there was around the suture.

Think about a tissue reaction around

the earth and a tissue reaction around the earth and moon. The tissue reaction around the earth is around the interface of the earth and the atmosphere. And then there is the moon on the side of the earth with a very similar reaction around its interface with substance and atmosphere.

Q. You answered the question at least seven or eight times today about whether more material implanted leads to an increased tissue reaction, and you said as a general proposition, that's true. Is that fair?

A. Yes, I think so. I think that's a general principle. Again, as I also mentioned, the details and particulars need to be determined on the basis of an implantation study.

Q. And -- and how much additional material -- strike that.

Are you able to evaluate the extent to which additional material creates a tissue response that's unacceptable from a preclinical study?

A. Yes. I think in every implantation study, one can make that determination.

Q. In your evaluation of all of the studies in the particle loss section of your

designation, the 38 studies over 43 years, did you find any unacceptable tissue response to any particles in those studies?

A. Yeah. The only --

MR. THORNBURGH: Objection.

THE WITNESS: The only studies that even talk about particles or fragments is the NDA work in a study done in 2002, Tab 33, that was done specifically to look at whether or not particles would be present after implantation of lengths of TVT tape. And, in fact, none were observed.

BY MR. THOMAS:

Q. Would you get 2260 in front of you, please. That's the Pariente study. I don't have the number of the rabbit study.

MR. THOMAS: Do you happen to have that, Dan?

MR. THORNBURGH: The test number or the exhibit number?

MR. THOMAS: The exhibit number. I do have it. I'm sorry.

MR. THORNBURGH: 2133.

BY MR. THOMAS:

Q. 2133. Can you get 2133 and 2260? 2133 is the March 5, 2003 rabbit test, and 2260 is

the Pariente study.

A. I've got the 2260. I'm looking for 2130.

Q. I'll get this copy to you.

A. Maybe it was discussed yesterday, and it's in this stack, yeah. I can probably get it, David.

Q. It's all right. I've got another copy.

The Pariente study is the particle loss study that counsel discussed with you at length at T-2260.

If you go to the first page of T-2260, down in the lower right-hand corner, it reads: Mechanical testing was performed with a 7-centimeter length sample (n=5) on an Instron 4466 with a 500-Newtons sensor using the software Series IX-7 to program the setup.

What is an Instron machine?

A. An Instron machine is a piece of equipment that can determine the tensile strength of a fiber by pulling at both ends and determining the strength at -- the force at which it breaks.

Q. And how did Pariente use an Instron machine to test the extent to which particles were

shed from the meshes that they tested?

A. Well, it looks like he put each mesh on the Instron machine and pulled it until it broke.

And as I look on Table 1 of that study, it looks like each of the meshes were pulled, as one might expect, a different peak load, depending on their biomechanical characteristics.

Q. And at what point in this process were particle loss measured? Are you able to tell that?

A. Could you repeat the question?

Q. Yes. At what point in this experiment were the particle losses measured?

A. I think at break.

Q. Okay.

A. I think at break. As I look at this Figure 3, there's a break, obviously, and then there's a drop in force because there is a break.

Q. Is 2260 a preclinical study that Ethicon conducts to evaluate particle loss?

A. Ethicon did not conduct this study.

Q. Does Ethicon -- strike that.

Is this a preclinical study?

A. This is kind of bench-top biomechanical testing.

Q. What is the difference between bench-top biomechanical testing and preclinical testing?

A. Well, I guess it can be considered preclinical because it's done before, you know, the product gets to clinic. But it's different than preclinical in my mind that has to do with in vitro or in vivo experimental studies with products in animals.

Q. Okay. And why is it important to you to measure products in vitro or in vivo in animals?

A. Well, because any bench-top is an artificial environment designed to look at a specific parameter under certain conditions. And in my mind, an in vivo study where there is an implantation of a product, it's more clinically relevant because it simulates the patient environment.

Q. If you look at T-2130, this is the two-week rabbit study; is that correct?

A. 2133?

Q. Yes.

A. Yes, a two-week rabbit study.

Q. And if you look at the abstract on Page 3, the objectives of the study were to compare

the mechanical strength and histological response of Prolene mesh and Prolene Soft mesh in skeletal muscle of the rabbit, correct?

A. Yes.

Q. And this is the same Prolene mesh that's used in TVT?

A. Yes, that's correct.

Q. And one of the specific endpoints of this study, this two-week rabbit study, T-2130, is to evaluate the extent to which the mesh shed particles inside the rabbit, correct?

A. Yes, that's correct.

Q. And how did the study do that?

A. The implant site was explanted and the tissue reaction was assessed. And, obviously, that would include the implant and any particulates that might be present, as that was one of the called out objectives in this particular experiment, although for me, any implantation study I would be looking for particulates, but this was called out in this study.

And so they would look at the tissue reaction to the mesh itself and any evidence of particulates in the surrounding tissue.

Q. If you go to Page 35 of that study,

T-2130?

A. That's 33. 2133?

Q. Yes.

A. You keep saying 30.

Q. I'm sorry. Thank you.

A. What was the page number?

Q. Page 35.

A. Okay.

Q. You see under the category, approximate average thickness of fibrous tissue located between the mesh fiber bundles -- strike that. Let me start over again.

On Page 35 of Exhibit T-2133, there is a table called "Histological Observations," correct?

A. Yes.

Q. And what are histological observations?

A. These are observations by the study pathologist looking at evidence of tissue reaction and integration and the evidence of fibrosis or any other impact of the surrounding tissues.

Q. And there is a category that's there. It says: Inflammatory cell infiltrates only associated with the mesh.

What is that? Right in the middle.

A. Yeah. It looks like they're calling out the tissue reaction associated with the mesh versus a tissue reaction to the skeletal muscle which was injured during the implantation process.

Q. And in the far right-hand corner -- excuse me -- the far right-hand column, there is a specific category for mesh particles within muscle.

And for each one of these animals, they specifically look in the histology to try to identify any particles that may have been in the rabbit in two weeks; is that correct?

A. That's correct.

Q. And do they find any particles in the histology for any of the rabbits?

A. No. No particles were observed for any -- for any -- at any implantation site.

Q. And this is a two-week study. Does the fact that this is a two-week study as opposed to a six-month study or a ten-year study have any impact on whether this is a valid study to determine the extent to which mesh particles may be found after implantation of mesh?

A. I think at a two-week post implantation period is sufficient time for a tissue

reaction and a fibrotic response to occur around any particulate if it were present.

Q. Okay. And the histology in this two-week rabbit study, 2133, was consistent with all of the other Prolene tissue response tests that you've gotten since 1964, correct?

A. Yeah, that's correct. If you look at the inflammatory cell --

MR. THORNBURGH: Objection. Sorry. If you can just give me a hair of a second --

THE WITNESS: I'm sorry.

MR. THORNBURGH: -- I'd appreciate it. I've got to get an objection in.

THE WITNESS: That's fine.

BY MR. THOMAS:

Q. Let me read the question again. And the histology in this two-week rabbit study, 2133, was consistent with all of the other Prolene tissue response tests that you've gotten since 1964, correct?

MR. THORNBURGH: Objection.

THE WITNESS: Yes. So if you look in the column, inflammatory cell infiltrates only associated with the mesh, for every mesh, that would

be Prolene Soft mesh, Prolene mechanical cut, which is TVT mesh, and Prolene ultrasonic cut mesh, which would be a laboratory-made device to simulate a different cutting process for TVT tape, all of the inflammatory reactions were minimal.

And, further, if you look at the approximate average thickness of fibrous tissue, what I would call fibrosis in studies that I've read, located between the mesh fiber bundles -- and this is measured -- attempted to be measured in microns, as we've seen in some early report -- pathology assessment schemes -- the results at 7 and 14 days are -- there's no distinct encapsulation for any product.

BY MR. THOMAS:

Q. What does that mean, no distinct encapsulation?

A. That the fibrotic response was relatively minimal.

Q. Let's talk about encapsulation quickly. I am jumping around a little bit, and I apologize.

In questions yesterday from counsel in -- with respect to T-2242, the exploratory 91-day tissue reaction study, there were some macroscopic

observations of encapsulation that were observed that were not confirmed upon histological review. Is that fair?

A. That's correct. I recall that discussion.

Q. And you were the person who conducted the histological review, correct?

A. Yes.

Q. And how is it that what might appear on a microscopic level to be encapsulation, upon histologic review, may prove something else altogether?

A. Yeah. The deficiency of a macroscopic observation is that it cannot see through the tissue. For example, if I were to put this piece of paper on top of this -- the title of this document, you would not see that.

That would be the result of a macroscopic observation. You could only see the surface. And that's a directional information, as I mentioned.

The histomorphological evaluation of the implant site looks at a cross-section of the implant, top to bottom, through and through. So not only can the pathologist see the surface coating,

but they can see all the other components through the mesh implant.

Q. Okay. So which is the more valid observation?

MR. THORNBURGH: Objection.

THE WITNESS: The histo -- the histomorphological evaluation is the definitive result.

BY MR. THOMAS:

Q. Okay. Sorry to jump around.

Going back to the Pariente study, which was T-2260, and the Ethicon two-week rabbit study, which is T-2133, which is the better study from a preclinical perspective for Ethicon to evaluate the safety and efficacy of its product?

A. I always lean towards in vivo studies to simulate a patient population.

Q. And what value to you in preclinical context is 2260, the Pariente study?

A. It's informational.

Q. Any value to you from a preclinical perspective other than what they state?

A. No.

Q. The next section in your disclosure is the porosity section. And the porosity section

for the development of mesh products only contains 12 entries. And counsel inquired at length about why you only had 12 studies to support the porosity testing for the TVT device.

And I think we've established pretty clearly that T-2247, the 1973 rabbit study, is the first study conducted by Ethicon on Prolene mesh for tissue reaction, correct?

A. Yes, that's correct.

Q. And we went through that study at some length.

Is the tissue reaction profile found in 2247 for Prolene mesh used in TVT consistent with the tissue reaction profile found in other Prolene mesh marketed by Ethicon?

MR. THORNBURGH: Objection.

THE WITNESS: First, is that exhibit that you called out the '73 study?

BY MR. THOMAS:

Q. Correct.

A. Then the response would be that the tissue reaction profile reported in the 1973 study represents the kind of tissue reaction seen in studies conducted since then.

Q. Including the 91-day rat study using

the 5 mil mesh?

A. That's correct.

Q. And in all of the porosity studies that are listed, the 12 that are listed here, the finding of tissue reaction with respect to Prolene mesh, does it meet the same profile?

A. Yes.

Q. And what is that profile?

A. A relatively mild reaction, an acute phase, which is transient and passes, because the implant is biocompatible. The tissue reaction transitions to a low level chronic inflammatory reaction and a fibrotic reaction that encapsulates elements in a three-dimensional way of the mesh.

And that tissue reaction is sustained through the -- for the duration of each of the studies, and in many of those studies, there is a diminution of that reaction over time.

Q. And that diminution in the reactions or the change in the reactions that you've just described is what you've described to counsel as a long-term chronic reaction?

A. That's correct.

Q. And does the long-term chronic reaction present any risk from a preclinical

perspective?

A. No.

MR. THORNBURGH: Objection.

BY MR. THOMAS:

Q. Now, you were questioned at some length about why you haven't done any more porosity studies on 6-mil Prolene mesh since the 1973 study. Why is that?

A. Well, there's -- in preclinical science, there are limitations on the number of animal studies that can be conducted. USDA animal welfare regulations require experimental institutions to justify the use of additional animals. And part of that justification is making a statement that this work has not been conducted previously, and if so, then further studies are not allowed.

Q. In the 91-day rat study, T-2242, there is an extensive section and literature research -- literature search contained in the data for that study. Do you recall that?

A. Yes.

Q. And why is that literature search set forth in that study?

A. Part of the --

MR. THORNBURGH: Objection.

THE WITNESS: Each research institution has an institutional animal care and use committee whose job is to have oversight over all experimental studies and as part of that oversight, requires a literature search of either the public -- well, the public and internal databases to make sure that previous studies that have been conducted will not be repeated.

BY MR. THOMAS:

Q. After Ethicon obtained the results from the test in 2247, which is a 1973 rabbit test, was there any reason to conduct further tissue reaction studies for this Prolene flat mesh?

A. No. And all tissue reactions conducted on various iterations of Prolene mesh over time showed a very comparable tissue reaction as described in the 1973 study.

Q. And so the 12 studies that you site in connection with your porosity analysis all have a consistent tissue reaction profile?

A. Yes.

Q. And is the tissue reaction profile that is described in those 12 studies consistent with the language in the IFU that you talked about

at length with counsel for the plaintiff?

MR. THORNBURGH: Objection.

THE WITNESS: Yes, I think so.

BY MR. THOMAS:

Q. The next category that you were asked about -- excuse me -- that you were designated on is Section BB. And you were asked to provide the specifics of all clinical, preclinical, and medical testing related to all of the TVT products, and you were responding to the preclinical piece of that.

Do you recall that?

A. Yes, I do.

Q. So as a part of that, you gathered all of the testing that Ethicon did for each of the devices. Is that fair?

A. That's correct.

Q. And to the extent that Ethicon leveraged prior testing from Prolene sutures, you've also identified that?

A. That's correct. They're all relevant.

Q. Okay. And you did that for the TVT device, correct?

A. Yes.

Q. You did that for the TVT-O device?